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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,149	MASON, R. PRESTON	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,29-56 and 60-68* is/are pending in the application.

4a) Of the above claim(s) *29-56 and 60-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 63-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed October 7, 2005 have been entered. Claims 7-28 and 57-59 have been cancelled. Claims 1-6, 29-56, and 60-68 are pending.

It is noted that claims 29-56 and 60-62 are withdrawn from further consideration by the examiner, 37 CFR 1 .142(b), as being drawn to a non-elected invention, of record in the previous Office Action dated November 4, 2004.

Claims 1-6 and 63-68 are examined herein to the extent they read on the elected invention and species.

The outstanding rejections under 35 USC 102 and 103 and double patenting rejections have been withdrawn in view of the applicant's remarks on the herein recited substantially pure form of the hydroxylated atorvastatin metabolites.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 63-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had full possession of the claimed invention. The claims herein are drawn to the use of any therapeutic agents represented by "hydroxylated atorvastatin metabolite". Thus, the recitation in the claims are deemed to a broad genus of any

compounds represented by "hydroxylated atorvastatin metabolite" which would reasonably be interpreted as any atorvastatins hydroxylated in any positions in atorvastatin and any atorvastatin metabolites. The specification as originally filed does not provide adequate support for a generic claims herein. The specification merely describes a single specific compound (see its structure at Fig 4A). The specification has not taught any other hydroxylated atorvastatin metabolites as intended to be encompassed within the scope of claims.

The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405 (emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the ad therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." at 1406 (emphases added).

More over, the court of In re CAFC held that "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when... the evidence indicates ordinary artisans could not predict the operability ... of any other species." (emphasis added, see In re CAFC 354. F.3d 1347, 69 USPQ2d 1274, Fed. Cir. 2ù04). The court of *Noelle v. Lederman* also pointed out that generic claim to anti-CD40CR Mabs lacked written description support because there was no description of anti-human or other species Mabs, an no description of

human CD40CR antigen. The court further pointed out that attempt to "define an unknown by its binding affinity to another unknown ' failed. See 355 F.3d 1343, 69 USPQ2d 1508, Fed. Cir. 2004.

In this case, the claimed composition herein is deemed not to adequately describe. Thus, ordinary artisans could not predict the operability of any other species of "hydroxylated atorvastatin metabolite". Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in full possession of the invention as it is now claimed.

Response to Arguments

Applicant's arguments filed October 7, 2005 averring the specification disclose the herein claimed substantially pure form of hydroxylated atorvastatin metabolites through US 5,385,929 have been fully considered but they are not persuasive. US patent 5,385,929 teaches only a specific hydroxylated atorvastatin compounds. Examiner notes that hydroxyl group can be attached to other phenyl ring. Since the instant claims do not specifically recite the position of the hydroxyl being attached to the specific phenyl rings, the recited hydroxylated atorvastatin compounds encompass more than what is disclosed in '929 patent. Therefore, the claims are still properly rejected under 35 USC 112, first paragraph. Applicants are encouraged to put forth the specific structures in the specification or in the claims according to 37 CFR 1.57(f) and (g).

Claim 68 is rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling the combination of amlodipine and atorvastatin metabolite further comprising the particular and specific antioxidants, does not reasonably provide enablement for any substances or compounds represented by "an endogenous and/or exogenous antioxidant" for the same reasons of record in the previous Office Action.

The instant specification fails to provide information that would allow the skilled artisan to practice the full scope of the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation as discussed in the previous Office Action.

Response to Arguments

Applicant's arguments filed October 7, 2005 averring the recited expression as not functional but descriptive have been fully considered but they are not persuasive. As the applicant realized, functional language define the invention's invention by its function but fails to disclose what the invention itself is. In the instant case, the applicant employs the terms that encompassing any compounds that having antioxidation activities (i.e., antioxidant) but fails to disclose what compounds might be encompassed by such broad terms. Examine notes that there is no structural information nor chemical information that would lead one of skilled in the art to elect suitable antioxidants to practice the instant invention. Without such guidance, any

compounds known to man are potential candidates for the instant invention. Therefore, one of skilled in the art would have to perform undue experimentation to ascertain the appropriate compounds and embodiments to practice the full scope of the claimed invention. The claims are properly rejected under 35 USC 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "effective derivative of amlodipine" recited in claims 2 and 3 renders the claims indefinite because it is not clear what compounds would be encompassed by the claims. The term "derivative" refers to any compounds that are derived from amlodipine, which is may be remotely similar to amlodipine in terms of structural, chemical, or pharmacological properties. Examiner notes that any compounds that are structurally similar to amlodipine may be derived from amlodipine. The instant specification does not even disclose any derivatives of amlodipine. Therefore, the claims are considered indefinite because one of ordinary skill in the art would not be able to determine the metes and bounds of the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 and 63-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO95/05822 ('822) and US 5,383,929 ('929).

'822 teaches amlodipine as effective in treating atherosclerosis (See the abstract and page 2, last two paragraphs).

'929 teaches the hydroxylated-atorvastatin compounds useful in inhibiting the biosynthesis of cholesterol (See col. 2, lines 24-35). '929 also teaches compounds that inhibiting the biosynthesis of cholesterol and is thus especially useful in treating atherosclerosis and hypercholesterolemia (See col. 1, lines 11-44).

The primary references do not expressly teach the hydroxylated-atorvastatin and amlodipine be incoported together into a single composition.

It would have been obvious to one of ordinary skill in the art at the time of invention to combine both amlodipine and hydroxylated-atorvastatin together in a single composition.

One of ordinary skill in the art would have been motivated to combine both amlodipine and hydroxylated-atorvastatin together in a single composition. Since they are known to be useful in treating atherosclerosis. Combining two agents, which are known to be useful to treat atherosclerosis individually, into a single composition useful for the very same purpose is prima facie obvious (See *In re Kerkhoven* 205 USPQ 1069).

Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over '822 and '929 as applied to claims 1-6 and 63-67 above, and further in view of Gilligan et al., reference of record.

'822 and '929 suggest the composition comprising amlodipine and hydroxylated atorvastatin.

'822 and '929 do not expressly teach the further incorporation of antioxidant.

Gilligan et al. teaches that antioxidants such as Vitamin A, C, and E, are known to be useful in the treatment of hypercholesterolemia in humans (See the abstract and entire article).

It would have been obvious to one of ordinary skill in the art at the time of invention to incorporate vitamin A, C, and E into the composition of amlodipine and hydroxylated-atorvastatin.

One of ordinary skill in the art would have been motivated to incorporate vitamin A, C, and E into the composition of amlodipine and hydroxylated-atorvastatin. Since vitamin A, C, and E are known to be useful in treating hypercholesterolemia, they would be useful in treating atherosclerosis. Further incorporation of vitamin A, C, and E into the atherosclerosis-treatment composition of amlodipine and hydroxylated-atorvastatin would be reasonably expected to increase the efficacy of atherosclerotic treating effect. Combining two or more agents, which are known to be useful to treat atherosclerosis individually, into a single composition useful for the very same purpose is prima facie obvious, at least additive effect is expected (See *In re Kerkhoven* 205 USPQ 1069).

Response to Arguments

Applicant's arguments with respect to claims 1-6 and 63-68 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617